

CLAIMS AMENDMENTS

Claims 1-16 (canceled).

Claim 17 (new): A method for determining the significance of a given nucleic acid polymorphism or mutation, in a nucleic acid molecule, on the structural properties of a protein encoded by said nucleic acid molecule comprising:

- (a) exposing the protein encoded by said nucleic acid molecule to a plurality of proteases;
- (b) determining an extent of proteolytic cleavage of said protein; and, optionally,
- (c) comparing said extent of proteolytic cleavage of the protein encoded by said nucleic acid molecule with an extent of proteolytic cleavage of a wild-type protein when exposed to said plurality of proteases.

Claim 18 (new): A screening method for determining the significance of a plurality of variants of at least one gene comprising:

- (a) obtaining a sample of at least one protein variant encoded by the plurality of variants of said at least one gene;
- (b) exposing said at least one protein variant to at least one protease;
- (c) determining an extent of proteolytic cleavage of said at least one protein variant; and
- (d) comparing said extent of proteolytic cleavage of said at least one protein

variant with an extent of proteolytic cleavage of a wild-type protein when exposed to the at least one protease.

Claim 19 (new): A method according to claim 18 wherein said at least one protein variant is exposed to a plurality of proteases.

Claim 20 (new): A method according to claim 19 wherein at least some of said plurality of proteases attack different sites within the at least one protein variant.

Claim 21 (new): A method according to claim 20 wherein said plurality of proteases are selected from the group consisting of trypsin, chymotrypsin, proteinase K, aminopeptidase, carboxypeptidase, collagenase, elastase, Kallikrein, metalloendopeptidase, papain, pepsin, and any combination thereof.

Claim 22 (new): A method according to claim 18 wherein a plurality of protein variants are exposed to said at least one protease.

Claim 23 (new): A method according to claim 22 wherein said plurality of protein variants are exposed to said at least one protease, or vice versa, simultaneously.

Claim 24 (new): A method according to claim 22 wherein said plurality of

protein variants are exposed to said at least one protease either simultaneously or successively.

Claim 25 (new): A method according to claim 22 wherein said plurality of protein variants are exposed to said at least one protease under conditions that support the activity of said at least one protease.

Claim 26 (new): A method according to claim 22 wherein digestion of said plurality of protein variants by said at least one protease is terminated by adding at least one protease inhibitor to the reaction.

Claim 27 (new): A method according to claim 18 wherein said extent of proteolytic cleavage is determined using a conventional protein assay.

Claim 28 (new): A method according to claim 27 wherein said protein assay involves SDS-PAGE analysis.

Claim 29 (new): A method according to claim 28 wherein said analysis is followed by staining or blotting.

Claim 30 (new): A method according claim 18 wherein additional studies are undertaken to determine the functionality of the at least one protein variant.

Claim 31 (new): A method according claim 18 wherein part (d) involves exposing the wild-type protein to said at least one protease, and then determining the extent of proteolytic cleavage of said wild-type protein.